

**Amendments to the Specification:**

Please replace paragraph [05] beginning at page 2, line 8, with the following:

--[05] Individual proteins can possess one or more discrete monomer domains. These proteins are often called mosaic proteins. For example, members of the LDL-receptor family contain four major structural domains: the cysteine rich A-domain repeats, epidermal growth factor precursor-like repeats, a transmembrane domain and a cytoplasmic domain. The LDL-receptor family includes members that: 1) are cell-surface receptors; 2) recognize extracellular ligands; and 3) internalize them for degradation by lysosomes. See Hussain et al., *The Mammalian Low-Density Lipoprotein Receptor Family*, (1999) Annu. Rev. Nutr. 19:141-72. For example, some members include very-low-density lipoprotein receptors (VLDL-R), apolipoprotein E receptor 2, LDLR-related protein (LRP) and megalin. Family members have the following characteristics: 1) cell-surface expression; 2) extracellular ligand binding consisting of A-domain repeats; 3) requirement of calcium for ligand binding; 4) recognition of receptor-associated protein and apolipoprotein (apo) E; 5) epidermal growth factor (EGF) precursor homology domain containing YWTD repeats (~~SEQ ID NO: 198~~) (SEQ ID NO:218); 6) single membrane-spanning region; and 7) receptor-mediated endocytosis of various ligands. See Hussain, *supra*. Yet, the members bind several structurally dissimilar ligands.

Please replace paragraph [13] beginning at page 3, line 24, with the following:

--[13] In some embodiments, the monomer domain is an LDL receptor class A domain monomer comprising the following sequence:

$C_aX_{3-15}C_bX_{3-15}C_cX_{6-7}C_d(D,N)X_4C_eX_{4-6}DEX_{2-8}C_f$  (SEQ ID NO:219)

wherein C is cysteine,  $X_{n-m}$  represents between n and m number of independently selected amino acids, and (D,N) indicates that the position can be either D or N; and wherein  $C_a$ - $C_c$ ,  $C_b$ - $C_e$  and  $C_d$ - $C_f$  form disulfide bonds.--

Please replace paragraph [14] beginning at page 3, line 30, with the following:

--[14] In some embodiments, the monomer domain is an LDL receptor class A domain monomer comprising the following sequence:

~~C<sub>a</sub>X<sub>6-7</sub>C<sub>b</sub>X<sub>4-5</sub>C<sub>c</sub>X<sub>6</sub>C<sub>d</sub>X<sub>5</sub>C<sub>e</sub>X<sub>8-10</sub>C<sub>f</sub>~~

C<sub>a</sub>X<sub>6-7</sub>C<sub>b</sub>X<sub>4-5</sub>C<sub>c</sub>X<sub>6</sub>C<sub>d</sub>X<sub>5</sub>C<sub>e</sub>X<sub>8-10</sub>C<sub>f</sub> (SEQ ID NOS:220-231)

wherein X is defined as follows:

C	X(6,7)	C	X(4,5)	C	X(6)	C	X(5)	C	X(8,10)	C
X1 X2 X3 X4 X5 X6	X1 X2 X3 X4	X1 X2 X3 X4 X5 X6	X1 X2 X3 X4 X5	X1 X2 X3 X4 X5 X6	X1 X2 X3 X4 X5	X1 X2 X3 X4 X5 X6 X7 X8				
A A A A A A C D D D D E E E E E F F F F F G G G G H H H H H I I I I K K K K K K L L L L L L M M M M M N N N N N P P P P P Q Q Q Q Q Q R R R R R R S S S S S S T T T T T T V V V V V V W W W Y Y Y Y	A A A C D D D D E E E E F F F G G G G H H H H I I I K K K K L L L L M M N N N N P P P P Q Q Q Q R R R R S S S S T T T T V V V Y Y	A A A A A A D D D D D E E E E E F F F F F G G G G G H H H H I I I I K K K K K K L L L L L L M M M M M N N N N N P P P P Q Q Q Q Q R R R R R S S S S S T T T T T V V V V V W W W Y Y Y Y Y	A A A A D D D D D E E E E E F F F G G G G G H H H H I I I I K K K K K K L L L L L L M M N N N N P P P P Q Q Q Q R R R R S S S S T T T T V V V W W Y Y	A A A D D D D D E E E E E F F F G G G G H H H H I I I K K K K L L L L M M N N N N P P P Q Q Q Q R R R S S S S S T T T T V V V W W W Y Y Y	A A A A A D D D D D E E E E E F F F G G G G H H H H I I I K K K K L L L L M M N N N N P P P Q Q Q Q R R R S S S S S T T T T V V V W W W Y Y Y	A A A A A A A D D D D D D E E E E E F F F G G G G H H H H I I I I K K K K K K L L L L L L M M M M N N N N N P P P P Q Q Q Q R R R R S S S S T T T T V V V W W Y Y Y				
X1 X2 X3 X4 X5 X6 X7	X1 X2 X3 X4 X5					X1 X2 X3 X4 X5 X6 X7 X8 X9 X10				
A A A A A D D D D D E E E E E F F F F F G G G G G H H H H H K K K K K L L L L L M M M M M N N N N N P P P P P Q Q Q Q Q R R R R R S S S S S T T T T T V V V V V W W Y	A A A A A D D D D D E E E E E F F F G G G G G H H H H I I I I K K K K K K L L L L L L M M N N N N P P P P Q Q Q Q R R R R S S S S T T T T V V V W W Y Y					A A A A A D D D D D E E E E E F F F G G G G H H H H I I I I K K K K K K L L L L L L M M M M N N N N N P P P P Q Q Q Q R R R R S S S S T T T T V V V W W Y Y				

In some embodiments, the LDL receptor class A domain monomers each comprise SEQ ID

NO:201 SEQ ID NO:331.--

Please replace paragraph [15] beginning at page 4, line 5, with the following:

--[15] In some embodiments, the monomer domain is an EGF domain monomer comprising the following sequence:

$C_aX_{3-14}C_bX_{3-7}C_cX_{4-16}C_dX_{1-2}C_eX_{8-23}C_f$  (SEQ ID NO:232)

wherein C is cysteine,  $X_{n-m}$  represents between n and m number of independently selected amino acids; and wherein  $C_a-C_c$ ,  $C_b-C_e$  and  $C_d-C_f$  form disulfide bonds.--

Please replace paragraph [16] beginning at page 5, line 1, with the following:

--[16] In some embodiments, the monomer domain is an EGF domain monomer comprising the following sequence:

$C_aX_{4-6}C_bX_{3-5}C_cX_{8-9}C_dX_1C_eX_{8-12}C_f$  (SEQ ID NOS:233-322)

wherein X is defined as follows:

Amdt. dated October 4, 2004

Reply to Notice to File Missing Parts of August 12, 2004

C	X(4,6)	C	X(3,5)	C	X(8,9)	C	X(1) C	X(8/12)	C
X1 X2 X3 X4	X1 X2 X3	X1 X2 X3 X4 X5 X6 X7 X8	X1	X1 X2 X3 X4 X5 X6 X7 X8					
A A A A	A A	A A A A A A A A	A	A A A A A A A A					
D D D D	D D	D D D D D D D D	D	D D D D D D D D					
E E E E	E E	E E E E E E E E	E	E E E E E E E E					
F F F F	F F	F F F F F F F F	F	F F F F F F F F					
G G G G	G G	G G G G G G G G	G	G G G G G G G G					
H H H H	H H	H H H H H H H H	H	H H H H H H H H					
I I I I	I I	I I I I I I I I	I	I I I I I I I I					
K K K K	K K	K K K K K K K K	K	K K K K K K K K					
L L L L	L L	L L L L L L L L	L	L L L L L L L L					
M M M M	M M	M M M M M M M M	M	M M M M M M M M					
N N N N	N N	N N N N N N N N	N	N N N N N N N N					
P P P P	P P	P P P P P P P P	P	P P P P P P P P					
Q Q Q Q	Q Q	Q Q Q Q Q Q Q Q	Q	Q Q Q Q Q Q Q Q					
R R R R	R R	R R R R R R R R	R	R R R R R R R R					
S S S S	S S	S S S S S S S S	S	S S S S S S S S					
T T T T	T T	T T T T T T T T	T	T T T T T T T T					
V V V V	V V	V V V V V V V V	V	V V V V V V V V					
W W W W	W W	W W W W W W W W	W	W W W W W W W W					
Y Y Y Y	Y Y	Y Y Y Y Y Y Y Y	Y	Y Y Y Y Y Y Y Y					
X1 X2 X3 X4 X5	X1 X2 X3 X4	X1 X2 X3 X4 X5 X6 X7 X8 X9	X1	X1 X2 X3 X4 X5 X6 X7 X8 X9 X10 X11 X12					
A A A A A	A A A A	A A A A A A A A A	A	A A A A A A A A A A					
D D D D	D D	D D D D D D D D	D	D D D D D D D D					
E E E E	E E	E E E E E E E E	E	E E E E E E E E					
F F F F	F F	F F F F F F F F	F	F F F F F F F F					
G G G G	G G	G G G G G G G G	G	G G G G G G G G					
H H H H	H H	H H H H H H H H	H	H H H H H H H H					
I I I I	I I	I I I I I I I I	I	I I I I I I I I					
K K K K	K K	K K K K K K K K	K	K K K K K K K K					
L L L L	L L	L L L L L L L L	L	L L L L L L L L					
M M M M	M M	M M M M M M M M	M	M M M M M M M M					
N N N N	N N	N N N N N N N N	N	N N N N N N N N					
P P P P	P P	P P P P P P P P	P	P P P P P P P P					
Q Q Q Q	Q Q	Q Q Q Q Q Q Q Q	Q	Q Q Q Q Q Q Q Q					
R R R R	R R	R R R R R R R R	R	R R R R R R R R					
S S S S	S S	S S S S S S S S	S	S S S S S S S S					
T T T T	T T	T T T T T T T T	T	T T T T T T T T					
V V V V	V V	V V V V V V V V	V	V V V V V V V V					
W W W W	W W	W W W W W W W W	W	W W W W W W W W					
Y Y Y Y	Y Y	Y Y Y Y Y Y Y Y	Y	Y Y Y Y Y Y Y Y					
X1 X2 X3 X4 X5 X6	X1 X2 X3 X4 X5	X1 X2 X3 X4 X5 X6 X7 X8							
A A A A A A	A A A A A	A A A A A A A A							
D D D D D D	D D D	D D D D D D							
E E E E E E	E E E	E E E E E E							
F F F F F F	F F F	F F F F F F							
G G G G G G	G G G	G G G G G G							
H H H H H H	H H H	H H H H H H							
I I I I I I	I I I	I I I I I I							
K K K K K K	K K K	K K K K K K							
L L L L L L	L L L	L L L L L L							
M M M M M M	M M M	M M M M M M							
N N N N N N	N N N	N N N N N N							
P P P P P P	P P P	P P P P P P							
Q Q Q Q Q Q	Q Q Q	Q Q Q Q Q Q							
R R R R R R	R R R	R R R R R R							
S S S S S S	S S S	S S S S S S							
T T T T T T	T T T	T T T T T T							
V V V V V V	V V V	V V V V V V							
W W W W W W	W W W	W W W W W W							
Y Y Y Y Y Y	Y Y Y	Y Y Y Y Y Y							

Please replace paragraph [28] beginning at page 7, line 32, with the following:

--[28] In some embodiments, the domains form a secondary structure by the formation of disulfide bonds. In some embodiments, the multimers comprise an A domain connected to a monomer domain by a polypeptide linker. In some embodiments, the linker is from 1-20 amino acids inclusive. In some embodiments, the linker is made up of 5-7 amino acids. In some embodiments, the linker is 6 amino acids in length. In some embodiments, the linker comprises the following sequence,  $A_1A_2A_3A_4A_5A_6$  (~~SEQ ID NO: 244~~) (SEQ ID NO:352), wherein  $A_1$  is selected from the amino acids A, P, T, Q, E and K;  $A_2$  and  $A_3$  are any amino acid except C, F, Y, W, or M;  $A_4$  is selected from the amino acids S, G and R;  $A_5$  is selected from the amino acids H, P, and R;  $A_6$  is the amino acid, T. In some embodiments, the linker comprises a naturally-occurring sequence between the C-terminal cysteine of a first A domain and the N-terminal cysteine of a second A domain.--

Please replace paragraph [42] beginning at page 10, line 11, with the following:

--[42] In some embodiments, the monomer domain is an LDL receptor class A domain monomer comprising the following sequence:

$C_aX_{3-15}C_bX_{3-15}C_cX_{6-7}C_d(D,N)X_4C_eX_{4-6}DEX_{2-8}C_f$  (SEQ ID NO:219)

wherein C is cysteine,  $X_{n-m}$  represents between n and m number of independently selected amino acids, and (D,N) indicates that the position can be either D or N; and wherein  $C_a-C_c$ ,  $C_b-C_e$  and  $C_d-C_f$  form disulfide bonds.--

Please replace paragraph [43] beginning at page 10, line 17, with the following:

--[43] In some embodiments, the monomer domain is an LDL receptor class A domain monomer comprising the following sequence:

~~C<sub>a</sub>X<sub>6-7</sub>C<sub>b</sub>X<sub>4-5</sub>C<sub>c</sub>X<sub>6</sub>C<sub>d</sub>X<sub>5</sub>C<sub>e</sub>X<sub>8-10</sub>C<sub>f</sub>~~

C<sub>a</sub>X<sub>6-7</sub>C<sub>b</sub>X<sub>4-5</sub>C<sub>c</sub>X<sub>6</sub>C<sub>d</sub>X<sub>5</sub>C<sub>e</sub>X<sub>8-10</sub>C<sub>f</sub> (SEQ ID NOS:220-231)

wherein X is defined as follows:

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Please replace paragraph [44] beginning at page 11, line 4, with the following:

--[44] In some embodiments, the monomer domain is an EGF domain monomer comprising the following sequence:

$C_aX_{3-14}C_bX_{3-7}C_cX_{4-16}C_dX_{1-2}C_eX_{8-23}C_f$  (SEQ ID NO:232)

wherein C is cysteine,  $X_{n-m}$  represents between n and m number of independently selected amino acids; and wherein  $C_a-C_c$ ,  $C_b-C_e$  and  $C_d-C_f$  form disulfide bonds.--

Please replace paragraph [45] beginning at page 12, line 1, with the following:

--[45] In some embodiments, the monomer domain is an EGF domain monomer comprising the following sequence:

$C_aX_{4-6}C_bX_{3-5}C_cX_{8-9}C_dX_1C_eX_{8-12}C_f$  (SEQ ID NOS:233-322)

wherein X is defined as follows:

C	X(4,6)	C	X(3,5)	C	X(8,9)	C	X(1)	C	X(8/12)	C
X1 X2 X3 X4	X1 X2 X3	X1 X2 X3 X4 X5 X6 X7 X8	X1	X1 X2 X3 X4 X5 X6 X7 X8	X1 X2 X3 X4 X5 X6 X7 X8 X9 X10 X11 X12					
A A A A	A A	A A A A A A A A	A	A A A A A A A A	A A A A A A A A A A					
D D D	D D	D D D D D D D	D	D D D D D D D	D D D D D D D					
E E E E	E	E E E E E E	E	E E E E E E	E E E E E E E					
F	F F	F F F F F F	F	F F F F F F	F F F F F F F					
G G G G	G G G	G G G G G G G	G	G G G G G G G	G G G G G G G					
H H H	H H H	H H H H H H H	H	H H H H H H H	H H H H H H H					
I	I	I I I I I I I	I	I I I I I I I	I I I I I I I					
K K K	K K	K K K K K K K	K	K K K K K K K	K K K K K K K					
L L L	L L	L L L L L L L	L	L L L L L L L	L L L L L L L					
M M M		M M M M M M M	M	M M M M M M M	M M M M M M M					
N N N N	N N N	N N N N N N N	N	N N N N N N N	N N N N N N N					
P P P P	P	P P P P P P P	P	P P P P P P P	P P P P P P P					
Q Q Q Q	Q Q Q	Q Q Q Q Q Q Q	Q	Q Q Q Q Q Q Q	Q Q Q Q Q Q Q					
R R R R	R R	R R R R R R R	R	R R R R R R R	R R R R R R R					
S S S S	S S S	S S S S S S S	S	S S S S S S S	S S S S S S S					
T T T T	T T T	T T T T T T T	T	T T T T T T T	T T T T T T T					
V V	V V	V V V V V V V	V	V V V V V V V	V V V V V V V					
W W		W W W W W W W	W	W W W W W W W	W W W W W W W					
Y Y	Y Y	Y Y Y Y Y Y Y	Y	Y Y Y Y Y Y Y	Y Y Y Y Y Y Y					
X1 X2 X3 X4 X5	X1 X2 X3 X4	X1 X2 X3 X4 X5 X6 X7 X8 X9		X1 X2 X3 X4 X5 X6 X7 X8 X9 X10 X11 X12						
A A A A A	A A A A	A A A A A A A A		A A A A A A A A A A						
D D D	D D D	D D D D D D D		D D D D D D D D D D						
E E F F F F	E E F F	E E E E E E E		E E E E E E E E E E						
G G G G G	G G G	G G G G G G G		G G G G G G G G G G						
H H H	H H H	H H H H H H H		H H H H H H H H H H						
I I I I	I I I	I I I I I I I		I I I I I I I I I I						
K K L L	K K L	K K K K K K K		K K K K K K K K K K						
L L M	L L M	L L L L L L L		L L L L L L L L L L						
M M N	M M N	M M M M M M M		M M M M M M M M M M						
N P P P	N P P	N P P P P P P		N P P P P P P P P P						
Q R R R	Q R R	Q R R R R R R		Q R R R R R R R R R						
S S S T	S S T	S S S S S S S		S S S S S S S S S S						
T V	T V	T T T T T T T		T T T T T T T T T T						
V W	V	V V V V V V V		V V V V V V V V V V						
Y Y	Y	Y Y Y Y Y Y Y		Y Y Y Y Y Y Y Y Y Y						
X1 X2 X3 X4 X5 X6	X1 X2 X3 X4 X5	X1 X2 X3 X4 X5 X6 X7 X8								
A A A A A A	A A A A A	A A A A A A A								
D D D D D	D D D	D D D D D								
E E F F F	E E F F	E E E E E								
F G G G G	F G G	F F F F F								
H H I I	H H I	H H H H H								
K K L L	K K L	K K K K K								
L M M	L M M	L L L L L								
N P P P	N P P	N N N N N								
Q R R R	Q R R	Q Q Q Q Q								
S S T V	S S T	S S S S S								
V W	V	V V V V V								
Y Y	Y Y	Y Y Y Y Y								

Please replace paragraph [57] beginning at page 18, line 14, with the following:

--[57] The present invention also provides non-naturally-occurring polypeptides comprising an LDL receptor class A domain monomer, wherein the monomer comprises the following sequence:

$C_aX_{3-15}C_bX_{3-15}C_cX_{6-7}C_d(D,N)X_4C_eX_{4-6}DEX_{2-8}C_f$  (SEQ ID NO:219)

wherein C is cysteine,  $X_{n-m}$  represents between n and m number of independently selected amino acids, and (D,N) indicates that the position can be either D or N; and wherein  $C_a-C_c$ ,  $C_b-C_e$  and  $C_d-C_f$  form disulfide bonds.--

Please replace paragraph [58] beginning at page 15, line 21, with the following:

--[58] In some embodiments, the monomer domain is an LDL receptor class A domain monomer comprising the following sequence:

$C_aX_{6-7}C_bX_{4-5}C_cX_6C_dX_5C_eX_{8-10}C_f$

$C_aX_{6-7}C_bX_{4-5}C_cX_6C_dX_5C_eX_{8-10}C_f$  (SEQ ID NOS:220-231)

wherein X is defined as follows:

C	X(6,7)						C	X(4,5)				C	X(6)						C	X(5)					C	X(8,10)										C
	X1	X2	X3	X4	X5	X6		X1	X2	X3	X4		X1	X2	X3	X4	X5	X6		X1	X2	X3	X4	X5		X1	X2	X3	X4	X5	X6	X7	X8			
	A	A	A	A	A	A		A	A		A	C		A	A	A	A	A			A	A	A			A	A	A		A	A					
	D	D	D	D		E		D	D	D	D	E		D	D	D	D	D		D	D	D	D	D		D	D	D	D	D	D	D				
	E	E	E	E	F	F		E	F	F	F	F	F	F	F	F	F	F		E	E	E	E	E		E	E	E	E	E	E	E				
	F	F	F	F	F	F		F	G	G	G	G	G	G	G	G	G	G		G	G	G	G	G		G	G	G	G	G	G	G				
	G	G	G	G	H	H		H	H	H	H	I	I	I	I	I	I	I		H	H	H	H	H		I	I	I	I	I	I	I				
	H	I	K	K	K	K		I	K	K	K	K	K	K	K	K	K	K		I	K	K	K	K		I	K	K	K	K	K	K				
	I	K	L	L	L	L		K	L	L	L	L	L	L	L	L	L	L		K	L	L	L	L		K	L	L	L	L	L	L				
	K	L	M	M	M	M		L	M	M	M	M	M	M	M	M	M	M		L	M	M	M	M		L	M	M	M	M	M	M				
	L	M	N	N	N	N		N	N	N	N	N	N	N	N	N	N	N		M	N	N	N	N		M	N	N	N	N	N	N				
	M	N	P	P	P	P		P	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q		N	Q	Q	Q	Q		N	Q	Q	Q	Q	Q	Q				
	N	P	Q	Q	Q	Q		Q	R	R	R	R	R	R	R	R	R	R		P	Q	Q	Q	Q		P	Q	Q	Q	Q	Q	Q				
	P	Q	R	R	R	R		Q	S	S	S	S	S	S	S	S	S	S		Q	R	R	R	R		Q	R	R	R	R	R	R				
	Q	R	S	S	S	S		R	T	T	T	T	T	T	T	T	T	T		R	S	S	S	S		R	S	S	S	S	S	S				
	R	S	T	T	T	T		S	V	V	V	V	V	V	V	V	V	V		S	T	T	T	T		S	T	T	T	T	T	T				
	S	T	V	V	V	V		T	W	W	W	W	W	W	W	W	W	W		T	V	V	V	V		T	V	V	V	V	V	V				
	T	V	W	W	W	W		V	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y		V	W	W	W	W		V	W	W	W	W	W	W				
	V	W	Y	Y	Y	Y		W	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y		W	Y	Y	Y	Y		W	Y	Y	Y	Y	Y	Y				
	W	Y	Y	Y	Y	Y		Y	Y																	Y	Y									
	Y	Y	Y	Y	Y	Y		Y	Y																	Y	Y									
	X1	X2	X3	X4	X5	X6	X7		X1	X2	X3	X4	X5													X1	X2	X3	X4	X5	X6	X7	X8	X9		
	A	A					A		A	A	A	A														A	A			A	A	A	A			
	D	D	D	D	D		E		D	D	D	D	D													D			D		D	D				
	E	E	E	E	E	F	E		E	E	E	E	E													E	E	E	E	E	E	E				
	F	F	F	F	F	G	F		F	F	F	F	F													F			F		F	F				
	G	G	G	G	G	H	G		G	G	G	G	G													G			G		G	G				
	H	H	H	H	H		H		H	H	H	H	H													H			H		H	H				
	I	K	K	K	K	L	K		I	K	K	K	K													I			I		I	I				
	K	L	L	L	L	L	L		K	L	L	L	L													K			K		K	K				
	L	L	L	L	L	L	L		L	L	L	L	L													L			L		L	L				
	M	M	M	M	M	M	M		M	M	M	M	M													M			M		M	M				
	N	N	N	N	N	N	N		N	N	N	N	N													N			N		N	N				
	P	P	P	P	P	P	P		P	P	P	P	P													P			P		P	P				
	Q	Q	Q	Q	Q	Q	Q		Q	Q	Q	Q	Q													Q			Q		Q	Q				
	R	R	R	R	R	R	R		R	R	R	R	R													R			R		R	R				
	S	S	S	S	S	S	S		S	S	S	S	S													S			S		S	S				
	T	T	T	T	T	T	T		T	T	T	T	T													T			T		T	T				
	V	V	V	V	V	V	V		V	V	V	V	V													V			V		V	V				
	W	W	W	W	W	W	W		W	W	W	W	W													W			W		W	W				
	Y	Y	Y	Y	Y	Y	Y		Y	Y																Y			Y		Y	Y				
	Y	Y	Y	Y	Y	Y	Y		Y	Y																Y			Y		Y	Y				
	X1	X2	X3	X4	X5	X6	X7	X8	X9	X10																X1	X2	X3	X4	X5	X6	X7	X8	X9	X10	
	A	A					A	A	A	A																A	A	A	A	A	A	A				
	D	D	D	D	D		D	D	D	D																D	D	D	D	D	D	D				
	E	E	E	E	E	F	E	E	E	E																E	E	E	E	E	E	E				
	F	F	F	F	F	G	F	F	F	F																F	F	F	F	F	F	F				
	G	G	G	G	G	H	G	G	G	G																G	G	G	G	G	G	G				
	H	H	H	H	H		H	H	H	H																H	H	H	H	H	H	H				
	I	K	K	K	K	L	K	K	K	K																I	K	K	K	K	K	K				
	K	L	L	L	L	L	K	L	L	L																K	L	L	L	L	L	L				
	L	L	L	L	L	L	L	L	L	L																L	L	L	L	L	L	L				
	M	M	M	M	M	M	M	M	M	M																M	M	M	M	M	M	M				
	N	N	N	N	N	N	N	N	N	N																N	N	N	N	N	N	N				
	P	P	P	P	P	P	P	P	P	P																P	P	P	P	P	P	P				
	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q																Q	Q	Q	Q	Q	Q	Q				
	R	R	R	R	R	R	R	R	R	R																R	R	R	R	R	R	R				
	S	S	S	S	S	S	S	S	S	S																S	S	S	S	S	S	S				
	T	T	T	T	T	T	T	T	T	T																T	T	T	T	T	T	T				
	V	V	V	V	V	V	V	V	V	V																V	V	V	V	V	V	V				
	W	W	W	W	W	W	W	W	W	W																W	W	W	W	W	W	W				
	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y																Y	Y	Y	Y	Y	Y	Y				

Please replace paragraph [60] beginning at page 16, line 7, with the following:

--[60] The present invention also provides non-naturally-occurring polypeptides comprising an EGF domain monomer, wherein the EGF domain monomer comprises the following sequence:

$C_aX_{3-14}C_bX_{3-7}C_cX_{4-16}C_dX_{1-2}C_eX_{8-23}C_f$  (SEQ ID NO:232)

wherein C is cysteine,  $X_{n-m}$  represents between n and m number of independently selected amino acids; and

wherein  $C_a-C_c$ ,  $C_b-C_e$  and  $C_d-C_f$  form disulfide bonds.--

Please replace paragraph [61] beginning at page 17, line 5, with the following:

--[61] In some embodiments, the monomer domain is an EGF domain monomer comprising the following sequence:

$C_aX_{4-6}C_bX_{3-5}C_cX_{8-9}C_dX_1C_eX_{8-12}C_f$  (SEQ ID NOS:233-322)

wherein X is defined as follows:

C	X(4,6)				C	X(3,5)			C	X(8,9)								C	X(1)	C	X(8/12)								C		
	X1	X2	X3	X4		X1	X2	X3		X1	X2	X3	X4	X5	X6	X7	X8		X1		X1	X2	X3	X4	X5	X6	X7	X8			
	A	A	A	A		A		A		A	A	A	A	A	A	A	A		A		A	A	A		A	A	A		A		
	D	D	D			D		D		D	D	D	D	D	D	D	D		D		D	D		D	D	D	D		D		
	E	E	E	E		E		E		E	E	E	E	E	E	E	E		E		E	E		E	E	E	E		E		
	F					F	F	F		F	F	F	F	F	F	F	F		F		F	F		F	F	F	F		F		
	G	G	G	G		G	G	G	H	G	G	G	G	G	G	G	G		G		G	G		G	G	G	G		G		
	H	H	H			H	H	H	I	H	H	H	H	H	H	H	H		H		H	H		H	H	H	H		H		
	I					I		I	I	I	I	I	I	I	I	I	I		I		I	I		I	I	I	I		I		
	K	K	K			K		K	K	K	K	K	K	K	K	K	K		K		K	K		K	K	K	K		K		
	L	L	L	M		L	L	L	L	L	L	L	L	L	L	L	L		L		L	L		L	L	L	L		L		
	M	M	M	M		M	M	M	M	M	M	M	M	M	M	M	M		M		M	M		M	M	M	M		M		
	N	N	N	N		N	N	N	N	N	N	N	N	N	N	N	N		N		N	N		N	N	N	N		N		
	P	P	P	P		P		P	P	P	P	P	P	P	P	P	P		P		P	P		P	P	P	P		P		
	Q	Q	Q	Q		Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q		Q		Q	Q		Q	Q	Q	Q		Q		
	R	R	R	R		R	R	R	R	R	R	R	R	R	R	R	R		R		R	R		R	R	R	R		R		
	S	S	S	T		S	S	T	T	S	S	S	S	S	S	S	S		S		S	S		S	S	S	S		S		
	T	T	T	T		T	T	T	T	T	T	T	T	T	T	T	T		T		T	T		T	T	T	T		T		
	V		V			V		V		V	V	V	V	V	V	V	V		V		V	V		V	V	V	V		V		
	W		W			W		W	W	W	W	W	W	W	W	W	W		W		W	W		W	W	W	W		W		
	Y		Y			Y	Y		Y	Y	Y	Y	Y	Y	Y	Y	Y		Y		Y	Y		Y	Y	Y	Y		Y		
	X1	X2	X3	X4	X5	X1	X2	X3	X4	X1	X2	X3	X4	X5	X6	X7	X8	X9		X1	X2	X3	X4	X5	X6	X7	X8	X9	X10	X11	X12
	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A		A	A		A	A	A	A	A	A	A	A	A
	D	D		D		D	D		D	D	D	D	D	D	D	D	D		D		D	D		D	D	D	D		D	D	D
	E	E	F	F	F	E	F	F	F	E	E	E	E	E	E	E	E	E		E		E	E		E	E	E	E		E	E
	G	G	G	G	G	G	G	G		G	G	G	G	G	G	G	G		G		G	G		G	G	G	G		G	G	G
	I	I	I	I	I	I	I	K	L	I	K	L	L	L	L	L	L		I		I	I		I	I	I	I		I	I	I
	K	K	L	L	L	K	L	L	L	K	L	L	L	L	L	L	L		K		K	K		K	K	K	K		K	K	K
	L	L	M	N	M	L	M	N	N	L	M	M	M	M	M	M	M		L		L	L		L	L	L	L		L	L	L
	M	M	N	N	N	M	N	N	N	M	M	M	M	M	M	M	M		M		M	M		M	M	M	M		M	M	M
	N	N	P	P	P	N	P	P	P	N	P	P	P	P	P	P	P		N		N	N		N	N	N	N		N	N	N
	P	P	Q	Q	Q	P	Q	Q	Q	P	Q	Q	Q	Q	Q	Q	Q		P		P	P		P	P	P	P		P	P	P
	Q	Q	R	R	R	Q	R	R	R	Q	R	R	R	R	R	R	R		Q		Q	Q		Q	Q	Q	Q		Q	Q	Q
	R	R	S	S	T	R	S	S	T	R	S	S	S	S	S	S	S		R		R	R		R	R	R	R		R	R	R
	S	S	T	T	T	S	T	T	T	S	T	T	T	T	T	T	T		S		S	S		S	S	S	S		S	S	S
	T		V		V	T	V		V	T	V	V	V	V	V	V	V		T		T	T		T	T	T	T		T	T	T
	V		W			V		W	W	W	W	W	W	W	W	W	W		W		W	W		W	W	W	W		W	W	W
	Y		Y		Y	Y	Y		Y	Y	Y	Y	Y	Y	Y	Y	Y		Y		Y	Y		Y	Y	Y	Y		Y	Y	Y

Please replace paragraph [62] beginning at page 18, line 1, with the following:

--[62] In some embodiments, the EGF domain monomer is fused to a heterologous amino acid sequence. In some embodiments, the monomer binds to a target molecule. In some embodiments, the polypeptide is 45 or fewer amino acids long. In some embodiments, the heterologous amino acid sequence is selected from an affinity peptide (e.g., SKVILF; SEQ ID NO:323), a heterologous LDL receptor class A domain, a heterologous EGF domain, a purification tag, an enzyme (e.g., horseradish peroxidase or alkaline phosphatase), and a reporter protein (e.g., green fluorescent protein or luciferase).--

Please replace paragraph [105] beginning at page 28, line 4, with the following:

--[105] Figure 2 schematically illustrates the alignment of partial amino acid sequence from a variety of the LDL-receptor class A-domains (SEQ ID NOS: 103, 100, 65, 117, 128, 21, 29, 39, 30, 77, 58, 50, and 14, respectively in order of appearance) ~~that include two human LRP1 sequences, two human LRP2 sequences, two human LDLR sequences, two human LDVR sequences, one human LRP3 sequence, one human MAT sequence, a human CO6 sequence, and a human SORL sequence,~~ to demonstrate the conserved cysteines. Consensus = SEQ ID NO:324.--

Please replace paragraph [106] beginning at page 28, line 10, with the following:

--[106] Figure 3, panel A schematically illustrates an example of an A-domain. Panel A schematically illustrates conserved amino acids in an A-domain of about 40 amino acids long (SEQ ID NO:325). The conserved cysteine residues are indicated by C, and the negatively charged amino acids are indicated by a circle with a minus ("-") sign. Circles with an "H" indicate hydrophobic residues. Panel B schematically illustrates two folded A-domains connected via a linker. Panel B also indicates two calcium binding sites, dark circles with Ca<sup>+2</sup>, and three disulfide bonds within each folded A-domain for a total of 6 disulfide bonds.--

Please replace paragraph [111] beginning at page 29, line 5, with the following:

--[111] Figure 8 depicts common amino acids in each position of the A domain (SEQ ID NO:326). The percentages above the amino acid positions refer to the percentage of naturally-occurring A domains with the inter-cysteine spacing displayed. Potential amino acid residues in bold depicted under each amino acid position represent common residues at that position. The final six amino acids, depicted as lighter-colored circles, represent linker sequences. The two columns of italicized amino acid residues at positions 2 and 3 of the linker represent amino acid residues that do not occur at that position. Any other amino acid (e.g., A, D, E, G, H, I, K, L, N, P, Q, R, S, T, and V) may be included at these positions.--

Please replace paragraph [112] beginning at page 29, line 13, with the following:

--[112] Figure 9 displays the frequency of occurrence of amino acid residues in naturally-occurring A domains for A domains with the following spacing between cysteines: CX<sub>6</sub>CX<sub>4</sub>CX<sub>6</sub>CX<sub>5</sub>CX<sub>8</sub>C (~~SEQ ID NO: 199~~) (SEQ ID NO:327).--

Please replace paragraph [113] beginning at page 29, line 16, with the following:

--[113] Figure 10 depicts an alignment of A domains (~~SEQ ID NO: 1-197~~) (SEQ ID NOS:1-217). At the top ~~and the bottom~~ of the figure, small letters (a-q) indicate conserved residues. ~~The predominant amino acids at these positions and the frequency with which they were observed in native A domains is illustrated at the bottom of the figure.--~~

Please replace paragraph [118] beginning at page 29, line 28, with the following:

--[118] Figure 15 is a graphical representation of the regions of sequence identity between the sequences of two different selected clones (SEQ ID NOS:328 and 329) and known human sequences from a database. The horizontal bars indicate areas of sequence identity



between the sequence of the selected clone and the human sequence and the numbers indicate the exact amino acid numbers that define the region of identity. The vertical arrow depicts an acceptable crossover sequence.--

Please replace paragraph [119] beginning at page 30, line 1, with the following:

--[119] Figure 16 illustrates cell killing induced by CD20-specific A domain monomers. SKVILF = SEQ ID NO:323.--

Please replace paragraph [140] beginning at page 33, line 14, with the following:

--[140] As described *supra*, monomer domains are optionally cysteine rich. Suitable cysteine rich monomer domains include, e.g., the LDL receptor class A domain ("A-domain") or the EGF-like domain. The monomer domains can also have a cluster of negatively charged residues. Optionally, the monomer domains contain a repeated sequence, such as YWTD (~~SEQ ID NO: 198~~) (SEQ ID NO:218) as found in the  $\beta$ -Propeller domain.--

Please replace paragraph [144] beginning at page 34, line 17, with the following:

--[144] Exemplary A domain sequences and consensus sequences are depicted in Figures 2, 3 and 8. Figure 9 displays location and occurrence of residues in A domains with the following spacing between cysteines. In addition, Figure 10 depicts a number of A domains and provides a listing of conserved amino acids. One typical consensus sequence useful to identify A domains is the following: C-[VILMA]-X<sub>(5)</sub>-C-[DNH]-X<sub>(3)</sub>-[DENQHT]-C-X<sub>(3,4)</sub>-[STADE]-[DEH]-[DE]-X<sub>(1,5)</sub>-C (~~SEQ ID NO: 200~~) (SEQ ID NO:330), where the residues in brackets indicate possible residues at one position. "X<sub>(#)</sub>" indicates number of residues. These residues can be any amino acid residue. Parentheticals containing two numbers refers to the range of amino acids that can occupy that position (e.g., "[DE]-X<sub>(1,5)</sub>-C" means that the amino acids DE are followed by 1, 2, 3, 4, or 5 residues, followed by C). This consensus sequence only

represents the portion of the A domain beginning at the third cysteine. A second consensus is as follows:  $C-X_{(3-15)}-C-X_{(4-15)}-C-X_{(6-7)}-C-[N,D]-X_{(3)}-[D,E,N,Q,H,S,T]-C-X_{(4-6)}-D-E-X_{(2-8)}-C$  (~~SEQ ID NO: 201~~) (SEQ ID NO:331). The second consensus predicts amino acid residues spanning all six cysteine residues. In some embodiments, A domain variants comprise sequences substantially identical to any of the above-described sequences.--

Please replace paragraph [145] beginning at page 34, line 32, with the following:

--[145] Additional exemplary A domains include the following sequence:

$C_aX_{3-15}C_bX_{3-15}C_cX_{6-7}C_d(D,N)X_4C_eX_{4-6}DEX_{2-8}C_f$  (SEQ ID NO:219)

wherein C is cysteine,  $X_{n-m}$  represents between n and m number of independently selected amino acids, and (D,N) indicates that the position can be either D or N; and wherein  $C_a$ - $C_c$ ,  $C_b$ - $C_e$  and  $C_d$ - $C_f$  form disulfide bonds.--

Please replace paragraph [146] beginning at page 35, line 4, with the following:

--[146] In some embodiments, the monomer domain is an LDL receptor class A domain monomer comprising the following sequence:

~~$C_aX_{6-7}C_bX_{4-5}C_cX_6C_dX_5C_eX_{8-10}C_f$~~

$C_aX_{6-7}C_bX_{4-5}C_cX_6C_dX_5C_eX_{8-10}C_f$  (SEQ ID NOS:220-231)

wherein X is defined as follows:

C	X(6,7)						C	X(4,5)				C	X(6)						C	X(5)					C	X(8,10)										C
X1	X2	X3	X4	X5	X6		X1	X2	X3	X4		X1	X2	X3	X4	X5	X6		X1	X2	X3	X4	X5		X1	X2	X3	X4	X5	X6	X7	X8				
A	A	A	A	A	A		A	A		A		A	A	A	A	A			A	A	A				A	A	A		A	A						
C																																				
D	D	D	D				D	D	D	D		D	D	D	D	D			D	D	D	D			D	D	D	D	D	D						
E	E	E	E		E		E	E	E	E		E	E	E	E	E			E	E	E	E			E	E	E	E	E							
F		F	F	F	F		F			F		F	F	F	F	F			F	F	F	F			F	F	F	F	F							
G	G	G	G				G	G	G	G		G	G	G	G	G			G	G	G	G			G	G	G	G	G	G						
H	H	H	H	H	H		H	H	H	H		H	H	H	H	H			H	H	H	H			H	H	H	H	H							
I				I	I		I					I							I						I											
K	K	K	K	K	K		K	K	K	K		K	K	K	K	K			K	K	K			K	K	K	K	K	K							
L	L	L	L	L	L		L		L	L		L	L	L	L	L			L	L	L	L			L	L	L	L	L	L						
M	M		M	M	M					M		M	M	M	M	M			M	M				M	M	M	M	M	M							
N	N	N	N		N		N	N	N	N		N	N	N	N	N			N	N	N	N			N	N	N	N	N	N						
P	P	P			P		P					P	P	P		P			P					P					P							
Q	Q	Q	Q	Q	Q		Q	Q	Q	Q		Q	Q	Q	Q	Q			Q	Q	Q	Q			Q	Q	Q	Q	Q							
R	R	R	R	R	R		R	R	R	R		R	R	R	R	R			R	R	R	R			R	R	R	R	R							
S	S	S	S	S	S		S	S	S	S		S	S	S	S	S			S	S	S	S			S	S	S	S	S							
T	T	T	T	T	T		T	T	T	T		T	T	T	T	T			T	T	T	T			T	T	T	T	T							
V	V	V	V	V	V		V	V		V		V	V	V	V	V			V	V	V	V			V	V	V	V	V							
W	W		W									W	W	W	W	W			W	W	W			W	W			W								
Y	Y	Y	Y				Y	Y				Y	Y	Y	Y	Y			Y	Y	Y			Y	Y			Y								

X1	X2	X3	X4	X5	X6	X7
A	A					A
D	D	D	D	D		
E	E		E	E		E
F		F	F		F	
G	G	G	G	G		G
H	H		H		H	
K		K	K	K		K
L	L	L		L	L	L
M			M			M
N	N	N	N	N		
P	P	P		P		
Q		Q			Q	
R	R	R	R	R		R
S	S	S	S			S
T	T	T	T			T
V	V	V	V			V
W					W	
Y					Y	

X1	X2	X3	X4	X5
A		A	A	A
D	D		D	
E			E	E
F				F
G	G			G
H		H		H
I		I		I
K	K	K	K	K
L	L	L	L	L
M			M	
N	N	N	N	N
P	P	P	P	P
Q	Q	Q	Q	Q
R	R	R	R	R
S	S	S	S	S
T	T	T	T	T
V	V		V	
W			W	
Y		Y		Y

X1	X2	X3	X4	X5	X6	X7	X8	X9
A		A				A	A	A
D	D			D			D	D
E				E	E	E	E	
F								F
G		G				G	G	
H		H				H		H
I								I
K								K
L								L
M							M	
N	N					N	N	N
P						P	P	P
Q		Q					Q	Q
R						R		R
S			S			S		S
T			T					T
V							V	
W								W
Y	Y						Y	

X1	X2	X3	X4	X5	X6	X7	X8	X9	X10
		A				A	A	A	A
D	D		D			D	D	D	
E		E			E	E	E	E	
F		F							F
G		G				G		G	
H						H	H	H	
I						I	I	I	
K		K				K	K	K	
L			L			L	L	L	
M						M	M	M	
N	N					N	N	N	
P						P	P	P	
Q		Q					Q	Q	
R						R		R	
S	S		S			S		S	
T			T					T	
V							V		
W							W		
Y							Y		Y

The table above indicates alternative amino acid residues at each position of the LDL receptor class A monomer domain. For example, there can be either 6 or 7 amino acids between cysteine C1 and cysteine C2. The upper left box of the table indicates alternative amino acid residues at each position if there are 6 amino acids between C1 and C2. The bottom left box in the table indicates alternative amino acid residues if there are seven amino acids between C1 and C2. In

all cases, the amino acid for one position (e.g., X1) is selected independently of the amino acids selected for remaining positions (e.g., X2, X3, etc.).--

Please replace paragraph [148] beginning at page 36, line 21, with the following:

--[148] Another exemplary monomer domain suitable for use in the practice of the present invention is the C2 domain. C2 monomer domains are polypeptides containing a compact  $\beta$ -sandwich composed of two, four-stranded  $\beta$ -sheets, where loops at the “top” of the domain and loops at the “bottom” of the domain connect the eight  $\beta$ -strands. C2 monomer domains may be divided into two subclasses, namely C2 monomer domains with topology I (synaptotagmin-like topology) and topology II (cytosolic phospholipase A2-like topology), respectively. C2 monomer domains with topology I contains three loops at the “top” of the molecule (all of which are  $\text{Ca}^{2+}$  binding loops), whereas C2 monomer domains with topology II contain four loops at the “top” of the molecule (out of which only three are  $\text{Ca}^{2+}$  binding loops). The structure of C2 monomer domains have been reviewed by Rizo and Südhof, *J. Biol. Chem.* 273;15879-15882 (1998) and by Cho, *J. Biol. Chem.* 276;32407-32410 (2001). The terms “loop region 1”, “loop region 2” and “loop region 3” refer to the  $\text{Ca}^{2+}$  binding loop regions located at the “top” of the molecule. This nomenclature, which is used to distinguish the three  $\text{Ca}^{2+}$  binding loops located at the “top” of the molecule from the non- $\text{Ca}^{2+}$  binding loops (mainly located at the “bottom” of the molecule) is widely used and recognized in the literature. See Rizo and Südhof, *J. Biol. Chem.* 273;15879-15882 (1998). Loop regions 1, 2, and 3 represent target binding regions and thus can be varied to modulate binding specificity and affinity. The remaining portions of the C2 domain can be maintained without alteration if desired. Some exemplary C2 domains are substantially identical to the following sequence (~~SEQ ID NO: 202~~) (SEQ ID NO:332):

Tyr	Ser	His	Lys	Phe	Thr	Val	Val	Val	Leu	Arg	Ala	Thr	Lys	Val
1				5					10					15
Thr	Lys	Gly	Ala	Phe	Gly	Asp	Met	Leu	Asp	Thr	Pro	Asp	Pro	Tyr
				20					25					30
Val	Glu	Leu	Phe	Ile	Ser	Thr	Thr	Pro	Asp	Ser	Arg	Lys	Arg	Thr
				35					40					45
Arg	His	Phe	Asn	Asn	Asp	Ile	Asn	Pro	Val	Trp	Asn	Glu	Thr	Phe
				50					55					60
Glu	Phe	Ile	Leu	Asp	Pro	Asn	Gln	Glu	Asn	Val	Leu	Glu	Ile	Thr
				65					70					75
Leu	Met	Asp	Ala	Asn	Tyr	Val	Met	Asp	Glu	Thr	Leu	Gly	Thr	Ala
				80					85					90
Thr	Phe	Thr	Val	Ser	Ser	Met	Lys	Val	Gly	Glu	Lys	Lys	Glu	Val
				95					100					105
Pro	Phe	Ile	Phe	Asn	Gln	Val	Thr	Glu	Met	Val	Leu	Glu	Met	Ser
				110					115					120
Leu	Glu	Val												
														123.

Residues 1-16, 29-48, 54-77 and 86-123 constitute positions located outside loop regions 1, 2 and 3 and residues 17-28, 49-53 and 78-85 constitute the loop regions 1, 2 and 3, respectively.--

Please replace paragraph [151] beginning at page 38, line 4, with the following:

--[151] Exemplary EGF monomer domains include the sequence:

$C_aX_{3-14}C_bX_{3-7}C_cX_{4-16}C_dX_{1-2}C_eX_{8-23}C_f$  (SEQ ID NO:232)

wherein C is cysteine,  $X_{n-m}$  represents between n and m number of independently selected amino acids; and

wherein  $C_a-C_c$ ,  $C_b-C_e$  and  $C_d-C_f$  form disulfide bonds.--

Please replace paragraph [152] beginning at page 38, line 9, with the following:

--[152] In some embodiments, the monomer domain is an EGF domain monomer comprising the following sequence:

$C_a X_{4-6} C_b X_{3-5} C_c X_{8-9} C_d X_1 C_e X_{8-12} C_f$  (SEQ ID NOS:233-322)

wherein X is defined as follows:

X(4,6)				X(3,5)			X(8,9)								X(1) C		X(8/12)								C				
X1	X2	X3	X4	X1	X2	X3	X1	X2	X3	X4	X5	X6	X7	X8	X1	X1	X2	X3	X4	X5	X6	X7	X8						
A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A						
D	D	D		D	D		D	D	D	D		D		D	D	D	D	D	D	D	D	D	D						
E	E	E	E	E	E		E	E	E	E	E		E		E	E	E	E	E	E	E	E	E						
F					F	F	F	F	F	F		F	F		F	F	F	F	F	F	F	F	F						
G	G	G	G		G	G	G	G	G	G		G		G	G	G	G	G	G	G	G	G	G						
H	H	H			H	H	H	H	H	H		H	H		H	H	H	H	H	H	H	H	H						
I					I							I		I	I	I	I	I	I	I	I	I	I						
K	K	K		K	K		K	K	K	K	K		K		K	K	K	K	K	K	K	K	K						
L	L	L		L	L		L	L	L	L	L		L		L	L	L	L	L	L	L	L	L						
M	M	M					M	M	M	M		M		M	M	M	M	M	M	M	M	M	M						
N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N						
P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P						
Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q						
R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R						
S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S						
T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T						
V		V			V		V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V						
W	W						W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W						
Y	Y	Y			Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y						
X1	X2	X3	X4	X5	X1	X2	X3	X4	X1	X2	X3	X4	X5	X6	X7	X8	X9	X1	X2	X3	X4	X5	X6	X7	X8	X9	X10	X11	X12
A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	
D	D	D	D		D	D		D	D	D	D	D	D		D		D	D	D	D	D	D	D	D	D	D	D	D	
E	E	E	E	F	E	E	F		E	E	E	E	E		E		E	E	E	E	E	E	E	E	E	E	E	E	
G	G	G	G		G	G			G	G	G	G	G		G		G	G	G	G	G	G	G	G	G	G	G	G	
H	H	H			H	H		H	H	H					H	H	H	H	H	H	H	H	H	H	H	H	H	H	
I	I	I	I		I				I						I		I	I	I	I	I	I	I	I	I	I	I	I	
K	K	K	K	K	K	K	K		K			K		K		K		K	K	K	K	K	K	K	K	K	K	K	
L	L	L	L	L	L	L	L		L	L	L	L	L		L		L	L	L	L	L	L	L	L	L	L	L	L	
M	M			M				M	M			M	M				M	M	M	M	M	M	M	M	M	M	M	M	
N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	
Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	
R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	
S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	
T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T	
V	V			V	V			V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	
W	W																												
Y	Y	Y	Y		Y			Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	

Please replace paragraph [209] beginning at page 59, line 25, with the following:

--[209] One example where the use of peptide linkers is widespread is for production of single-chain antibodies where the variable regions of a light chain ( $V_L$ ) and a heavy chain ( $V_H$ ) are joined through an artificial linker, and a large number of publications exist within this particular field. A widely used peptide linker is a 15mer consisting of three repeats of a Gly-Gly-Gly-Gly-Ser (~~SEQ ID NO: 240~~) (SEQ ID NO:333) amino acid sequence ((Gly<sub>4</sub>Ser)<sub>3</sub>) (SEQ ID NO:334). Other linkers have been used, and phage display technology, as well as, selective infective phage technology has been used to diversify and select appropriate linker sequences (Tang *et al.* (1996), *J. Biol. Chem.* 271, 15682-15686; Hennecke *et al.* (1998), *Protein Eng.* 11, 405-410). Peptide linkers have been used to connect individual chains in hetero- and homo-dimeric proteins such as the T-cell receptor, the lambda Cro repressor, the P22 phage Arc repressor, IL-12, TSH, FSH, IL-5, and interferon- $\gamma$ . Peptide linkers have also been used to create fusion polypeptides. Various linkers have been used and in the case of the Arc repressor phage display has been used to optimize the linker length and composition for increased stability of the single-chain protein (Robinson and Sauer (1998), *Proc. Natl. Acad. Sci. USA* 95, 5929-5934).--

Please replace paragraph [211] beginning at page 60, line 10, with the following:

--[211] Still another way of obtaining a suitable linker is by optimizing a simple linker, e.g. (Gly<sub>4</sub>Ser)<sub>n</sub> (~~SEQ ID NO: 240~~) (SEQ ID NO:335), through random mutagenesis.--

Please replace paragraph [212] beginning at page 60, line 12, with the following:

--[212] As mentioned above, it is generally preferred that the peptide linker possess at least some flexibility. Accordingly, in some embodiments, the peptide linker contains 1-25 glycine residues (SEQ ID NO:336), 5-20 glycine residues (SEQ ID NO:337), 5-15 glycine residues (SEQ ID NO:338) or 8-12 glycine residues (SEQ ID NO:339). The peptide linker will



typically contain at least 50% glycine residues, such as at least 75% glycine residues. In some embodiments of the invention, the peptide linker comprises glycine residues only.--

Please replace paragraph [213] beginning at page 60, line 18, with the following:

--[213] The peptide linker may, in addition to the glycine residues, comprise other residues, in particular residues selected from the group consisting of Ser, Ala and Thr, in particular Ser. Thus, one example of a specific peptide linker includes a peptide linker having the amino acid sequence Gly<sub>x</sub>-Xaa-Gly<sub>y</sub>-Xaa-Gly<sub>z</sub> (~~SEQ ID NO: 203~~), wherein each Xaa is independently selected from the group consisting Ala, Val, Leu, Ile, Met, Phe, Trp, Pro, Gly, Ser, Thr, Cys, Tyr, Asn, Gln, Lys, Arg, His, Asp and Glu, and wherein x, y and z are each integers in the range from 1-5 (SEQ ID NO:340). In some embodiments, each Xaa is independently selected from the group consisting of Ser, Ala and Thr (SEQ ID NO:341), in particular Ser (SEQ ID NO:342). More particularly, the peptide linker has the amino acid sequence Gly-Gly-Gly-Xaa-Gly-Gly-Gly-Xaa-Gly-Gly-Gly (~~SEQ ID NO: 204~~), wherein each Xaa is independently selected from the group consisting Ala, Val, Leu, Ile, Met, Phe, Trp, Pro, Gly, Ser, Thr, Cys, Tyr, Asn, Gln, Lys, Arg, His, Asp and Glu (SEQ ID NO:343). In some embodiments, each Xaa is independently selected from the group consisting of Ser, Ala and Thr (SEQ ID NO:344), in particular Ser (SEQ ID NO:345).--

Please replace paragraph [217] beginning at page 61, line 20, with the following:

--[217] In a further embodiment, the peptide linker comprises glycine residues and cysteine residue, such as glycine residues and cysteine residues only. Typically, only one cysteine residue will be included per peptide linker. Thus, one example of a specific peptide linker comprising a cysteine residue, includes a peptide linker having the amino acid sequence Gly<sub>n</sub>-Cys-Gly<sub>m</sub> (~~SEQ ID NO: 205~~), wherein n and m are each integers from 1-12 (SEQ ID NO:346), e.g., from 3-9, from 4-8, or from 4-7. More particularly, the peptide linker may have the amino acid sequence GGGGG-C-GGGGG (~~SEQ ID NO: 206~~) (SEQ ID NO:347).--

Please replace paragraph [218] beginning at page 61, line 27, with the following:

--[218] This approach (i.e. introduction of an amino acid residue comprising an attachment group for a non-polypeptide moiety) may also be used for the more rigid proline-containing linkers. Accordingly, the peptide linker may comprise proline and cysteine residues, such as proline and cysteine residues only. An example of a specific proline-containing peptide linker comprising a cysteine residue, includes a peptide linker having the amino acid sequence  $\text{Pro}_n\text{-Cys-Pro}_m$  (~~SEQ ID NO: 207~~), wherein n and m are each integers from 1-12 (SEQ ID NO:348), preferably from 3-9, such as from 4-8 or from 4-7. More particularly, the peptide linker may have the amino acid sequence  $\text{PPPPP-C-PPPPP}$  (~~SEQ ID NO: 208~~) (SEQ ID NO:349).--

Please replace paragraph [222] beginning at page 62, line 20, with the following:

--[222] A specific example of a peptide linker comprising an *in vivo* N-glycosylation site is a peptide linker having the amino acid sequence  $\text{Gly}_n\text{-Asn-Xaa-Ser/Thr-Gly}_m$  (~~SEQ ID NO: 209~~) (SEQ ID NO:350), preferably  $\text{Gly}_n\text{-Asn-Xaa-Thr-Gly}_m$  (~~SEQ ID NO: 210~~) (SEQ ID NO:351), wherein Xaa is any amino acid residue except proline, and wherein n and m are each integers in the range from 1-8, preferably in the range from 2-5.--

Please replace paragraph [226] beginning at page 63, line 12, with the following:

--[226] A linker can be a native or synthetic linker sequence. An exemplary native linker includes, e.g., the sequence between the last cysteine of a first LDL receptor A domain and the first cysteine of a second LDL receptor A domain can be used as a linker sequence. Analysis of various A domain linkages reveals that native linkers range from at least 3 amino acids to fewer than 20 amino acids, e.g., 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or 18 amino acids long. However, those of skill in the art will recognize that longer or shorter linker sequences can be used. An exemplary A domain linker sequence is depicted in Figure 8.

In some embodiments, the linker is a 6-mer of the following sequence A<sub>1</sub>A<sub>2</sub>A<sub>3</sub>A<sub>4</sub>A<sub>5</sub>A<sub>6</sub> (SEQ ID NO: 244) (SEQ ID NO:352), wherein A<sub>1</sub> is selected from the amino acids A, P, T, Q, E and K; A<sub>2</sub> and A<sub>3</sub> are any amino acid except C, F, Y, W, or M; A<sub>4</sub> is selected from the amino acids S, G and R; A<sub>5</sub> is selected from the amino acids H, P, and R; and A<sub>6</sub> is the amino acid, T.--

Please replace paragraph [330] beginning at page 96, line 15, with the following:

--[330] In order to detect serum levels of A-domains in the serum samples, an enzyme linked immunosorbent assay (ELISA) was performed. Therefore, wells of a maxisorp 96 well microtiter plate (NUNC, Denmark) were coated with each 1 µg anti-His<sub>6</sub> (SEQ ID NO:358)-antibody in TBS containing 2 mM CaCl<sub>2</sub> for 1 h at 4 C. After blocking remaining binding sites with casein (Sigma) solution for 1 h, wells were washed three times with TBS containing 0.1 % Tween and 2 mM CaCl<sub>2</sub>. Serial concentration dilutions of the serum samples were prepared and incubated in the wells for 2 h in order to capture the a-domain proteins. After washing as before, anti-HA-tag antibody coupled to horse radish peroxidase (HRP) (Roche Diagnostics, 25 µg/ml) was added and incubated for 2 h. After washing as described above, HRP substrate (Pierce) was added and the detection reaction developed according to the instructions of the manufacturer. Light absorption, reflecting the amount of a-domain protein present in the serum samples, was measured at a wavelength of 450 nm. Obtained values were normalized and plotted against a time scale.--

Please replace paragraph [334] beginning at page 97, line 11, with the following:

--[334] The following list (SEQ ID NOS:353-357) provides sequences of monomer domains analyzed in this example.

```
IG156  CLSSEFQCQSSGRCIPLAWVCDGDNDCRDDSDEKSKPRT
RBCA   CRSSQFQCNDRIPIGRWRCDGDNDQDGSDETGGDSHILPFSTPGPST
RBCB   CPAGEFPCKNGQCLPVTWLCDGVNCLDGSDEKGGRPFGPGATSAPAA
RBC11  CPPDEFPCCKNGQIPQDWLCDGVNCLDGSDEKDCGRPGPGATSAPAA
CSA-A8 CGAGQFPCKNGHCLPLNLLCDGVNCEDNSDEPSELCKALT--
```

Please replace paragraph [336] beginning at page 97, line 22, with the following:

--[336] Anti-6xHis (SEQ ID NO:358) antibody was immobilized by hydrophobic interaction to a 96-well plate (Nunc). Serial dilutions of serum from each blood sample were incubated with the immobilized antibody for 3 hours. Plates were washed to remove unbound protein and probed with  $\alpha$ -HA-HRP to detect monomer.--

Please replace paragraph [338] beginning at page 97, line 29, with the following:

--[338] One monkey was injected subcutaneously per pool, at a dose of 0.25 mg/kg/monomer in 2.5 mL total volume in saline. Blood samples were drawn at 24, 48, 96, and 120 hours. Anti-6xHis (SEQ ID NO:358) antibody was immobilized by hydrophobic interaction to a 96-well plate (Nunc). Serial dilutions of serum from each blood sample were incubated with the immobilized antibody for 3 hours. Plates were washed to remove unbound protein and separately probed with  $\alpha$ -HA-HRP,  $\alpha$ -FLAG-HRP,  $\alpha$ -ETag-HRP, and  $\alpha$ -myc-HRP to detect the monomer.--

Please replace paragraph [344] beginning at page 98, line 29, with the following:

--[344] A library of DNA sequences encoding monomeric C2 domains is created by assembly PCR as described in Stemmer *et al.*, *Gene* 164, 49-53 (1995). The oligonucleotides used in this PCR reaction are (SEQ ID NOS: 211-223 SEQ ID NOS:359-371, respectively, in order of appearance):

```
5' -acactgcaatcgcgcttacggctCCCGGGCGGATCCTcccataaagttca
5' -agctaccaaagtgacannknnknnknnknnknnknnknnknnknnknnknnkccatacgtcgaattgttca t
5' -agctaccaaagtgacaaaaggtgcttttggtgatatggttgatactccagatccatacgtcgaattgttca t
5' -taggaagagaacacgctcattttnnknnknnkattaaccctggttggaacgagacctttgagt
5' -taggaagagaacacgctcattttaataatgatattaaccctggttggaacgagacctttgagt
5' -ttggaatcaccctaatagnknnknnknnknnknnknnknnknnknnknnknnkactctaggtacagcaa
5' -ttggaatcaccctaataggatgcaaattatggttatggacgaaactctaggtacagcaa
5' -aagaaggaagtcccattttattttcaatcaagttactgaaatggtcttagagatgtccctt
5' -tgtcacttttggtagctcttaacacaactacagtgaacttatgggaGGA
5' -acgtgttctcttcttagaatctggagttgtactgatgaacaattcgacgta
5' -attaggggtgatttccaaaacattttcttgattaggtatctaataaaactcaaaggtctcggt
```

5' -atgggacttccttcttttctccactttcattgaagatacagtaaacggttgctgtacctagagt  
5' -gaccgatagcttgccgattgcagtggtGCCACAGAGGCCTCGAGaacttcaagggacatctctaaga--

Please replace paragraph [349] beginning at page 99, line 31, with the following:

--[349] The oligonucleotides used in this PCR reaction are (~~SEQ ID NOS: 224-225~~ SEQ ID NOS: 372 and 373, respectively, in order of appearance):

5' -acactgcaatcgcgcccttacggctCAGgtgCTGgtggttcccataagtctactgta  
5' -gaccgatagcttgccgattgcagtcAGcacCTGaaccaccaccaccagaaccaccaccaccaacttcaa  
gggacatctcta (linker sequence is underlined).--

Please replace paragraph [350] beginning at page 99, line 37, with the following:

--[350] PCR fragments are then digested with AlwNI, digestion products are separated on 1.5% agarose gel and C2 domain fragments are purified from the gel. Subsequently, PCR fragments are multimerized by DNA ligation in the presence of stop fragments. The stop fragments are listed below:

Stop1 (~~SEQ ID NO: 226~~) (SEQ ID NO: 374):

5' -gaattcaacgctactaccattagtagaattgatgccaccttttcagctcgcgcccaaat  
gaaaaaatggtcaaactaaatctactcgtttcgcagaattgggaatcaactgttacatggaatgaaacttccagacac  
cgtactttatgaatatattatgacgattccgagggcgcgcccggaactaccggtatgatgttcgggattatgccccggga  
tcttcaggtgctg-3' (digested with EcoRI and AlwNI).

Stop2 (~~SEQ ID NO: 227~~) (SEQ ID NO: 375):

5' -caggtgctgcactcgaggccactgcggccgcatattaacgtagatttttcctccc  
aacgtcctgactggtataatgagccagttcttaaaatcgcataaccagtagatggtgattaaagttgaaattaaacc  
gtctcaagagctttgttacgttgatttgggtaaatgaagctt-3' (digested with AlwNI and HindIII).--

Please replace paragraph [352] beginning at page 100, line 11, with the following:

--[352] Multimers are separated on 1% agarose gel and DNA fragments corresponding to ~~stop1-C2-C2-stop2~~ Stop1-C2-C2-Stop2 are purified from the gel. ~~Stop1-C2-C2-stop2~~ Stop1-C2-C2-Stop2 fragments are PCR amplified using primers 5' aattcaacgctactaccat-3' (~~SEQ ID NO: 242~~) (SEQ ID NO: 376) and 5'-agcttcattacccaaatcaac-3' (~~SEQ ID NO: 243~~) (SEQ ID NO: 377) and subsequently digested with BamHI and XhoI. Optionally, the

polynucleotides encoding the multimers can be put through a further round of affinity screening (e.g., FACS analysis as described above).--

Please replace paragraph [355] beginning at page 100, line 24, with the following:

--[355] A library of DNA sequences encoding monomeric A domains is created by assembly PCR as described in Stemmer *et al.*, *Gene* 164, 49-53 (1995). The oligonucleotides used in this PCR reaction are (~~SEQ ID NOS: 228-235~~ SEQ ID NOS:378-385, respectively, in order of appearance):

5' - CACTATGCATGGACTCAGTGTGTCCGATAAGGGCACACGGTGCCTACCCGTATGATGTTCCGGATTATGCC  
CCGGGCAGTA  
5' - CGCCGTCGCATMSCMAGYKCNSAGRAATACAWYGGCCGYTWYYGCACBKAAATTSGYYAGVCNSACAGGTA  
CTGCCCCGGGGCAT  
5' - CGCCGTCGCATMSCMATKCCNSAGRAATACAWYGGCCGYTWYYGCACBKAAATTSGYYAGVCNSACAGGTA  
CTGCCCCGGGGCAT  
5' - ATGCGACGGCGWWRATGATTGTSVAGATGGTAGCGATGAAVWGRRTTGTVMAVNMVNMVGCCVTACGGGCT  
CGGCCTCT  
5' - ATGCGACGGCGWCCGGATTGTSVAGATGGTAGCGATGAAVWGRRTTGTVMAVNMVNMVGCCVTACGGGCT  
CGGCCTCT  
5' - ATGCGACGGCGWWRATGATTGTSVAGATAACAGCGATGAAVWGRRTTGTVMAVNMVNMVGCCVTACGGGCT  
CGGCCTCT  
5' - ATGCGACGGCGWCCGGATTGTSVAGATAACAGCGATGAAVWGRRTTGTVMAVNMVNMVGCCVTACGGGCT  
CGGCCTCT  
5' - TCCTGGTAGTACTTATCTACTACTATTTGTCTGTGTCTGCTCTGGGTTCTTAACGGTTCGGCCACAGAGGC  
CGAGCCCGTA

where R=A/G, Y=C/T, M=A/C, K=G/T, S=C/G, W=A/T, B=C/G/T, D=A/G/T, H=A/C/T,  
V=A/C/G, and N=A/C/G/T.--

Please replace paragraph [359] beginning at page 101, line 19, with the following:

--[359] The oligonucleotides used in this PCR reaction are:

5'-aagcctcagcgaccgaa (~~SEQ ID NO: 236~~) (SEQ ID NO:386)  
5'-agcccaataggaacccat (~~SEQ ID NO: 237~~) (SEQ ID NO:387)--

Please replace paragraph [360] beginning at page 101, line 22, with the following:

--[360] PCR fragments are digested with AlwNI and BglI. Digestion products are separated on 3% agarose gel and A domain fragments are purified from the gel. PCR fragments are multimerized by DNA ligation in the presence of the following stop fragments:  
Stop1 (~~SEQ ID NO: 238~~) (SEQ ID NO:388):

5' -gaattcaacgctactaccattagtagaattgatgccaccttttcagctcgcgccccaaatgaaaaaatggt  
caaactaaatctactcgttcgcagaattgggaatcaactgttacatggaatgaaacttcagacaccgtactttatg  
aatatttatgacgattccgaggcgcgcccggactaccgctatgatgttcggattatgccccgggaggatccagtac  
ctg-3'

(digested with EcoRI and ALwNI)

Stop2 (~~SEQ ID NO: 239~~) (SEQ ID NO:389):

5' -gccctacgggcctcgaggcacctggtgcggccgcataattaacgtagatttttctcccaacgtcctgactg  
gtataatgagccagttcttaaaatcgcataaccagtacatggtgattaaagttgaaattaaaccgtctcaagagctt  
tgttacgttgatttgggtaatgaagctt-3'

(digested with BglI and HindIII).--

Please replace paragraph [362] beginning at page 102, line 1, with the following:

--[362] Multimers are separated on 1% agarose gel and DNA fragments corresponding to ~~stop1-A-A-A-stop2~~ Stop1-A-A-A-Stop2 are purified from the gel. Stop1-A-A-A-stop2 Stop1-A-A-A-Stop2 fragments are subsequently PCR amplified using primers 5'-agcttcattacccaatcaac-3' (SEQ ID NO:390) and 5' aattcaacgctactaccat-3' (SEQ ID NO:391) and subsequently digested with XmaI and SfiI. Selected polynucleotides are then cloned into a phage expression system and tested for affinity for the target protein.--

Please replace paragraph [367] beginning at page 102, line 24, with the following:

--[367] Clones which showed differential binding were sequenced (Table 1) and cloned into expression vectors with SKVILF (SEQ ID NO:323) peptides fused N- and C-terminally. Protein was produced and purified according to standard methods.--

Please replace paragraph [368] and Table 1 beginning at page 102, line 27, with the following:

--[368] Raji or Daudi cells were incubated in fresh RPMI medium supplemented with 10% FBS in the presence or absence of purified monomers for 6 hours at 37°C. Dead cells were stained with trypan blue and counted visually using a hemocytometer (Figure 16).

Table 1: CD20 binding sequences (SEQ ID NOS:392-406)

2	CLPDEFQCRSTGICIPLAWRCDGVNDCQDDSDETNCRATGRT
3	CLPGEFRCRGTSICIPPSWVCDGVDDCGDGSDEALEHCGDSHILPFSTPGPST
4	CQPNEFP CGSTGLCVPREWLC DGVDDC QDGSDEPD CGDSHILPFSTPGPST
5	CLPGEFRCRGTSICIPPSWVCDGVDDCGDGSDEALEHCGDSHILPFSTPGPST
6	CRSGEFKCHGTRPCVPQRWVCDGDDDCVDGSDEKSCETPARR
7	CRSSQFKCHNTRPCIPGRWVCDGVNDCLDGSDEANCRRAARR
8	CLPERFQCAVPGYCIPLPGVCDGVNDCQEDSDEPNCRAPGLR
9	CRRNEFRCKSGHCVPQPLVCDGVRD CEDNSDEPSCGRPGPGATSAPAA
10	CRAGEFPCKNGQCLPVTWLC DGVNDC LDGSDEKGCGRPGPGATSAPAA
11	CPSNEFTCKSGHCVPQPFVCDGVPD CEDNSDETS CGRPGPGATSAPAA
14	CRASEFP CRGTGT CIPRHWLC DGENDC ADSSDEKDCGRPGPGATSAPAA
15	CPPDEFRCRCKSYKRCVPLAFVCDGVDDCEDGSDEEGCGRPGPGATSAPAA
1	CLPDEFQCRSTGICIPLAWRCDGVNDCQDDSDETNCRATGRT
6	CPAGEFQCGNGQCI PATWLC DGVNDC LDNSDETGC SQDPEFHKV
CC3	CPASQFKCHNTRTCIPRRWVCDGVNDCLDGSDEANCRRAAPT--

Please replace paragraph [374] and Table 2 beginning at page 103, line 36, with the following:

--[374] Positive clones were genetically fused to create direct homodimers, with and without insertion of a 12 amino-acid repeated Gly-Gly-Ser linker (SEQ ID NO:407) between the domains, using standard molecular biology techniques, and were cloned into an expression vector. Protein was produced and purified using standard techniques. Protein was assayed for its ability to mimic natural TPO activity in a TF1 cell proliferation assay (Figure 18).



**Table 2: TPO-R Binding Sequences (SEQ ID NOS:408-411)**

T4690 (TPO1) CHSTGEFRCSRSSGICVSPTWVCDGENDCLDGSDEASCTAAGPT  
T5 (TPO2) CPPSEFRCSNGQCI PREWRCDGDNDCADNSDEESCSAPASEPPGSLSLQ  
T2 (TPO9) CLPSEFRCSNGHCIPRRWRCDGEPDCQDGSDEANCGTSEHTSLQ  
T1 (TPO10) CQSNEFQCHNYNICLPRPWVCDGVNDPCDGSDEEGCSAPASEPPGSLSLQ--

Please replace paragraph [382] and Table 3 beginning at page 105, line 5, with the following:

--[382] Phage were selected on serial dilutions 2 additional times. Individual clones were sequenced (Table 3).

**Table 3 : IgE-Binding Monomer Sequences**

IGE-1  
CPANEFQCRNSSTCIPRRWLC DGDDDCGDGSDETGCSAPASEPPGSLSLQ (SEQ ID NO:412)

**Walked Dimers**

1  
CPANEFQCRNSSTCIPRRWLC DGDDDCGDGSDETGCSAPASEPPGSL  
CQPDQFRCSNGRCLSRWLC DGEDDCEDDSDETD CPTRTSLQ (SEQ ID NO:413)

2  
CPANEFQCRNSSTCIPRRWLC DGDDDCGDGSDETGCSAPASEPPGSL  
CLPSQFP CDSGNCLPLTWLC DGVDCCGDNSDEEDCSAPASEPPGSLSLQ (SEQ ID NO:414)

3  
CPANEFQCRNSSTCIPRRWLC DGDDDCGDGSDETGCSAPASEPPGSL  
CRANQFP CDNGNCLPQWRCDGDND CVDGSDETSCEAPAHTSLQ (SEQ ID NO:415)

4  
CPANEFQCRNSSTCIPRRWLC DGDDDCGDGSDETGCSAPASEPPGSL  
CAPNEFQCRDNTCLPEDWRCDGEDDCADNSDEANCTTPGPTSLQ (SEQ ID NO:416)

5  
CPANEFQCRNSSTCIPRRWLC DGEDDCEDGSDEASDTCSAPASEPPGSL  
CPANEFQCRNSSTCIPRRWLC DGDDDCGDGSDETGCSAPASEPPGSLSLQ (SEQ ID NO:417)

6  
CGSGQFP CGSGHCVPLNWVCDGVDDCGDDSDETDCKAHT  
CPANEFQCRNSSTCIPRRWLC DGDDDCGDGSDETGCSAPASEPPGSLSLQ (SEQ ID NO:418)

7  
CPANEFQCRNSSTCIPRRWLC DGDDDCGDGSDETGCSAPASEPPGSL  
CGADQFP CSSGHCIPLPWVCDGEDDCADGSDEADCRGTEPTSLQ (SEQ ID NO:419)

8  
CPANEFQCRNSSTCIPRRWLC DGDDDCGDGSDETGCSAPASEPPGSL  
CAPSQFR CNGRCIPRSWRCDGEDDCADDSDEENC SAPASEPPGSLSLQ (SEQ ID NO:420)

9  
RVWRRLVGS  
CRPNQFTCKSSETCIPAHWRCDGDDDCGDGSDEADCTETRT  
CPANEFQCRNSSTCIPRRWLC DGDDDCGDGSDETGCSAPASEPPGSLSLQ (SEQ ID NO:421)

10  
CPANEFQCRNSSTCIPRRWLC DGDDDCGDGSDETGCSAPASEPPGSL  
CQSSQFP CHDYEICLPATLLCDGVDDCLDGSDETNCAKPTSLQ (SEQ ID NO:422)

12

CPANEFQCRNSSTCIPRRWLCDGDDDCGDGSDEPGCSAPASEPPGSL  
CPPGEFPCGNRSVPLTWLCDGVDDCGDNSDETGCETTGRSLQ (SEQ ID NO:423)

13 (27)

CGSNQFPCENGNCVPLGWGCDGVNDCQDNSDESLATCGRPGPGATSAPAA  
CPANEFQCRNSSTCIPRRWLCDGDDDCGDGSDETGCAPASEPPGSLSLQ (SEQ ID NO:424)

14

CPSGQFPCCDNHGCIPRRWLCDGEDDCPDGSDEAQVCQORT  
CPANEFQCRNSSTCIPRRWLCDGDDDCGDGSDETGCAPASEPPGSLSLQ (SEQ ID NO:425)

15

CPANEFQCRNSSTCIPRRWLCDGDDDCGDGSDETGCAPASEPPGSLSLQ  
ALLCDGVDDCRDGSDESALCEEHT  
CPANEFQCRNSSTCIPRRWLCDGDDDCGDGSDETGCAPASEPPGSLSLQ (SEQ ID NO:426)

16

CPANEFQCRNSSTCIPRRWLCDGDDDCGDGSDEPGCSAPASEPPGSL  
CRRAEFTCRNGSCLPVPWLCDAEENDCPDGSDEPDGSPARRSLQ (SEQ ID NO:427)

19

CPANEFQCRNSSTCIPRRWLCDGDDDCGDGSDEPGCSAPASEPPGSL  
CPPDQFRCKNGRCIPRHLVCDGDDDCGDSDSDEAGCQTRTSLQ (SEQ ID NO:428)

21

CPANEFQCRNSSTCIPRRWLCDGDDDCGDGSDETGCAPASEPPGSL  
CEPGQFQCNNNDTCVSPWLCDADRDGSRSDRPPHCATPELTSLQ (SEQ ID NO:429)

23

CPAGQFRCENGRCCLPPWRCGDGVNDCEDNSDEAGCGDSHILPFSTPGPST  
CPANEFQCRNSSTCIPRRWLCDGDDDCGDGSDETGCAPASEPPGSLSLQ (SEQ ID NO:430)

25

CPANEFQCRNSSTCIPRRWLCDGDDDCGDGSDEPGCSAPASEPPGSL  
CLSSQFRCENGQCIPLTWGC DGDDDCQDGSDETNCPTRTSLQ (SEQ ID NO:431)

26

CPANEFQCRNSSTCIPRRWLCDGDDDCGDGSDETGCSPVPT  
CPANEFQCRNSSTCIPRRWLCDGDDDCGDGSDETGCAPASEPPGSLSLQ (SEQ ID NO:432)

27 (13)

CGSNQFPCENGNCVPLGWGCDGVNDCQDNSDESLATCGRPGPGATSAPAA  
CPANEFQCRNSSTCIPRRWLCDGDDDCGDGSDETGCAPASEPPGSLSLQ (SEQ ID NO:424)

30

CPANEFQCRNSSTCIPRRWLCDGDDDCGDGSDEPGCSAPASEPPGSL  
CAASQFRCNNNSRCLPPPLGCDGVDDCGDNSDEADCGRPGPGATSAPAASLQ (SEQ ID NO:433)

31

CPANEFQCRNSSTCIPRRWLCDGDDDCGDGSDETGCAPASEPPGSL  
CPANEFQCRNSSTCIPRRWLCDGEDDCGDGSDETGCAPASEPPGSLSLQ (SEQ ID NO:434)--

Please replace paragraph [384] beginning at page 106, line 32, with the following:

--[384] A library of DNA sequences encoding monomeric A domains was created by assembly PCR as described in Stemmer *et al.*, *Gene* 164:49-53 (1995). The oligonucleotides used in this PCR reaction are (SEQ ID NOS:435-465):

```
5' -ATTCTCACTCGGCCGACGGTGCCTACCCGT-3'
5' -ACGGTGCCTACCCGTATGATGTTCCGGATTATGCCCCGGGTCTGGAGGCGTCTGGTGGTTCGTGT-3'
5' -CGCCGTCGCAAMSCMASBBBCNSTGRAABGCATNTKYYGKWAYYSYKGCATYYAAATTBGBYGRDAGVKTBACACGAACC
ACAGA-3'
5' -CGCCGTCGCAAMSCMASBBBCNSTGRAABGCAKYKCCGYTKYYGCATYYAAATTBGBYGRDAGVKTBACACGAACCACCAGA-3'
5' -CGCCGTCGCAAMSCMASBBBCNSTGRAABGCATNTKYYGKWAYYSYKGCACBKGAAC TSGYYCGVCNSACA
CGAACCAACAGA-3'
5' -CGCCGTCGCAAMSCMASBBBCNSTGRAABGCAKYKCCGYTKYYGCACBKGAAC TSGYYCGVCNSACACGAACCACCAGA-3'
5' -TTGCGACGGCGWWRATGATTGTSNGGACRRCTCGGATGAA-3'
5' -TTGCGACGGCGWWRATGATTGTSNGGACGGCTCGGATGAA-3'
5' -TTGCGACGGCGWWRATGATTGTSRGGACRRCTCGGATGAA-3'
5' -TTGCGACGGCGWCCGGATTGTSNGGACRRCTCGGATGAA-3'
5' -TTGCGACGGCGWCCGGATTGTSNGGACRRCTCGGATGAA-3'
5' -TTGCGACGGCGWCCGGATTGTSRGGACRRCTCGGATGAA-3'
5' -AGGCCTGCAATGACGTABGCKBTKBACAGYTKYTTTCATCCGAGYGTCC-3'
5' -AGGCCTGCAATGACGTABGTNCGGNSSYTBACAGYTKYTTTCATCCGAGYGTCC-3'
5' -AGGCCTGCAATGACACTTTGTGAAATTCGGATCCTGGCTACAGYTKYTTTCATCCGAGYGTCC-3'
5' -AGGCCTGCAATGACAGGGAACCCGGCGGTTTCAGATGCTGGCGCGCTACAGYTKYTTTCATCCGAGYGTCC-3'
5' -AGGCCTGCAATGACGCTGCCGGTGCAAGTCGCACCTGGGCCCGGACGACACAGYTKYTTTCATCCGAGYGTCC-3'
5' -AGGCCTGCAATGACGTGCTCGGACCTGGGGTGCTAAACGGCAGAAATGAGAATCACCACAGYTKYTTTCATCCGAGYGTCC-3'
5' -AGGCCTGCAATGACGTABGCKBTKBACAMWSCKSCGVTTTCATCCGAGCCGTCC-3'
5' -AGGCCTGCAATGACGTABGTNCGGNSSYTBACAMWSCKSCGVTTTCATCCGAGCCGTCC-3'
5' -AGGCCTGCAATGACACTTTGTGAAATTCGGATCCTGGCTACAMWSCKSCGVTTTCATCCGAGCCGTCC-3'
5' -AGGCCTGCAATGACAGGGAACCCGGCGGTTTCAGATGCTGGCGCGCTACAMWSCKSCGVTTTCATCCGAGCCGTCC-3'
5' -AGGCCTGCAATGACGCTGCCGGTGCAAGTCGCACCTGGGCCCGGACGACACAMWSCKSCGVTTTCATCCGAGCCGTCC-3'
5' -AGGCCTGCAATGACGTGCTCGGACCTGGGGTGCTAAACGGCAGAAATGAGAATCACCACAMWSCKSCGVTTTCATCCGAGC
CGTCC-3'
5' -AGGCCTGCAATGACGTABGCKBTKBACAGDKWKCCRRCGVTTTCATCCGAGYGTCC-3'
5' -AGGCCTGCAATGACGTABGTNCGGNSSYTBACAGDKWKCCRRCGVTTTCATCCGAGYGTCC-3'
5' -AGGCCTGCAATGACACTTTGTGAAATTCGGATCCTGGCTACAGDKWKCCRRCGVTTTCATCCGAGYGTCC-3'
5' -AGGCCTGCAATGACAGGGAACCCGGCGGTTTCAGATGCTGGCGCGCTACAGDKWKCCRRCGVTTTCATCCGAGYGTCC-3'
5' -AGGCCTGCAATGACGCTGCCGGTGCAAGTCGCACCTGGGCCCGGACGACACAGDKWKCCRRCGVTTTCATCCGAGYGTCC-3'
5' -AGGCCTGCAATGACGTGCTCGGACCTGGGGTGCTAAACGGCAGAAATGAGAATCACCACAGDKWKCCRRCGVTTTCATCCGAGY
TCC-3'
5' -TGAATTTTCTGTATGAGTTTGTCTAAACAACCTTTCAACAGTTTCGGCCCCAGAGGCTGCAATGAC-3'
(R=A/G, Y=C/T, M=A/C, K=G/T, S=C/G, W=A/T, B=C/G/T, D=A/G/T, H=A/C/T, V=A/C/G, and
N=A/C/G/T) _--
```

Please replace paragraph [387] beginning at page 107, line 29, with the following:

--[387] Phage from the final eluate was used directly, without purification, as a template to PCR amplify A domain encoding DNA sequences. The oligonucleotides used in this PCR reaction are:

```
5' -aagcctcagcgaccgaa (SEQ ID NO:466)
5' -agcccaataggaacccat (SEQ ID NO:467) --
```

Please replace paragraph [392] beginning at page 108, line 12, with the following:

--[392] Binding of the individual phage clones to their target proteins was analyzed by ELISA. Clones yielding the highest ELISA signals were sequenced and subsequently recloned into a protein expression vector. Exemplary sequences are provided below (SEQ ID NOS:468-475):

>CD28-A1  
CGPGRFQCESGQCIPATWVCDGENDCVDDSDSEKSCATTAPTCLPDQFQCHDYRRCIPLGWVCDGVPDCVDNSDEANC  
EPPT

>CD28-A2  
CGPGRFQCESGQCIPATWVCDGENDCVDDSDSEKSCATTAPTCPPDQFTCN SGRCVPLNWLCDGVNDCADSSDEPPEC  
QPR T

>CD28-A10  
CGPGRFQCESGQCV PATWVCDGDDDCADGSDEKSCATTAPTCE SNQFQCGSGQCLPGTWRC DGVNDCADSSDETGC G  
RPGPGATSAPAACGPGRFQC NNGNCVPQTLGCDGDND CGDSSDEANCSAPASEPPGSL

>CD28-A4  
CGPGRFQCESGQCIPATWVCDGENDCVDDSDSEKSCATTAPTC PANQFQCGNGRCIPPAWLCDGVNDCGDGSDESQ LC  
AATGPT

>CD28-A5  
CGPGRFQCESGQCIPATWVCDGENDCVDDSDSEKSCATTAPTCLPNEFRCSNGQCIPPNWRCDGVDDCRDGSDEAGCS  
QDPEFHKV

>CD28-A7  
CGPGRFQCESGQCIPATWVCDGENDCVDDSDSEKSCATTAPT C GSGQFRC SNGNCLPLRLGCDGVDDCGDSSDEPLDP  
CAATVRT

>CD28-A17  
CGPGRFQCESGQCIPATWVCDGENDCVDDSDSEKSCATTAPT C P SGQFKCNSGRCVPPNWLCDGVNDCPDNSDEANCP  
PRT

>CD28-A19  
CGPGRFQCESGQCIPATWVCDGENDCVDDSDSEKSCATTAPT C Q ADEFQCQSSGKCLPVNWVCDGDND CGDSSDETNC  
ATTGRT--

Please replace paragraph [398] beginning at page 110, line 13, with the following:

--[398] A library of DNA sequences encoding monomeric A domains was created by assembly PCR as described in Stemmer *et al.*, *Gene* 164:49-53 (1995). The oligonucleotides used in this PCR reaction are (SEQ ID NOS:476-506):

```
5' -ATTCTCACTCGGCCGACGGTGCCTACCCGT-3'
5' -ACGGTGCCTACCCGTATGATGTTCCGGATTATGCCCCGGGTCTGGAGGCTCTGGTGGTTCGTGT-3'
5' -CGCCGTCGCAAMSCMASBBBCNSTGRAABGCATNTKYYGKWAYYSYKGCATYYAAATTBGBYGRDAGVKTACACGAACC
  ACCAGA-3'
5' -CGCCGTCGCAAMSCMASBBBCNSTGRAABGCAKYKCGCGYTKYYGCATYYAAATTBGBYGRDAGVKTACACGAACCACCAGA-3'
5' -CGCCGTCGCAAMSCMASBBBCNSTGRAABGCATNTKYYGKWAYYSYKGCACBKGAACSTSGYYCGVCNSACA
  CGAACCAACCAGA-3'
5' -CGCCGTCGCAAMSCMASBBBCNSTGRAABGCAKYKCGCGYTKYYGCACBKGAACSTSGYYCGVCNSACACGAACCACCAGA-3'
5' -TTGCGACGGCGWWRATGATTGTSNGGACRRCTCGGATGAA-3'
5' -TTGCGACGGCGWWRATGATTGTSNGGACGGCTCGGATGAA-3'
5' -TTGCGACGGCGWWRATGATTGTSRGGACRRCTCGGATGAA-3'
5' -TTGCGACGGCGWCCGGATTGTSNGGACRRCTCGGATGAA-3'
5' -TTGCGACGGCGWCCGGATTGTSNGGACGGCTCGGATGAA-3'
5' -TTGCGACGGCGWCCGGATTGTSRGGACRRCTCGGATGAA-3'
5' -AGGCCTGCAATGACGTABGCKBTKBACAGYYTKYTTTCATCCGAGYYGTCC-3'
5' -AGGCCTGCAATGACGTABGTNCGNSSYTBACAGYYTKYTTTCATCCGAGYYGTCC-3'
5' -AGGCCTGCAATGACACTTTGTGAAATTCGGATCCTGGCTACAGYYTKYTTTCATCCGAGYYGTCC-3'
5' -AGGCCTGCAATGACAGGGAACCCGGCGGTTTCAGATGCTGGCGCGCTACAGYYTKYTTTCATCCGAGYYGTCC-3'
5' -AGGCCTGCAATGACGCTGCCGGTGCAGAGTTCGACCTGGGCCCCGACGACCACAGYYTKYTTTCATCCGAGYYGTCC-3'
5' -AGGCCTGCAATGACGTGCTCGGACCTGGGGTGCTAAACGGCAGAATATGAGAATCACCACAGYYTKYTTTCATCCGAGYYGTCC-3'
5' -AGGCCTGCAATGACGTABGCKBTKBACAMWSCKSCGVTTTCATCCGAGCCGTCC-3'
5' -AGGCCTGCAATGACGTABGTNCGNSSYTBACAMWSCKSCGVTTTCATCCGAGCCGTCC-3'
5' -AGGCCTGCAATGACGCTGCCGGTGCAGAGTTCGACCTGGGCCCCGACGACCACAMWSCKSCGVTTTCATCCGAGCCGTCC-3'
5' -AGGCCTGCAATGACGCTGCCGGTGCAGAGTTCGACCTGGGCCCCGACGACCACAMWSCKSCGVTTTCATCCGAGCCGTCC-3'
5' -AGGCCTGCAATGACGTGCTCGGACCTGGGGTGCTAAACGGCAGAATATGAGAATCACCACAMWSCKSCGVTTTCATCCGAGC
  CGTCC-3'
5' -AGGCCTGCAATGACGTABGCKBTKBACAGDKWKCCRRCGVTTTCATCCGAGYYGTCC-3'
5' -AGGCCTGCAATGACGTABGTNCGNSSYTBACAGDKWKCCRRCGVTTTCATCCGAGYYGTCC-3'
5' -AGGCCTGCAATGACACTTTGTGAAATTCGGATCCTGGCTACAGDKWKCCRRCGVTTTCATCCGAGYYGTCC-3'
5' -AGGCCTGCAATGACAGGGAACCCGGCGGTTTCAGATGCTGGCGCGCTACAGDKWKCCRRCGVTTTCATCCGAGYYGTCC-3'
5' -AGGCCTGCAATGACGCTGCCGGTGCAGAGTTCGACCTGGGCCCCGACGACCACAGDKWKCCRRCGVTTTCATCCGAGYYGTCC-3'
5' -AGGCCTGCAATGACGTGCTCGGACCTGGGGTGCTAAACGGCAGAATATGAGAATCACCACAGDKWKCCRRCGVTTTCATCCGAGYYG
  TCC-3'
5' -TGAATTTCTGTATGAGGTTTGTCTAAACAACTTTCAACAGTTTCGGCCCCAGAGCCTGCAATGAC-3'
(R=A/G, Y=C/T, M=A/C, K=G/T, S=C/G, W=A/T, B=C/G/T, D=A/G/T, H=A/C/T, V=A/C/G, and
N=A/C/G/T) _--
```

Please replace paragraph [401] beginning at page 111, line 15, with the following:

--[401] Phage from the final eluate was used directly, without purification, as a template to PCR amplify A domain encoding DNA sequences. The oligonucleotides used in this PCR reaction are:

```
5' -aagcctcagcgaccgaa (SEQ ID NO:466)
5' -agcccaataggaacccat (SEQ ID NO:467)--
```

Please replace paragraph [404] beginning at page 111, line 25, with the following:

--[404] Clones were identified by the same methods as those described above for CD28. Identified clones included the following (SEQ ID NOS:507-511):

>IL6#4 >IL6#4

CLSSQFQCKNGQCIPQTWVCDGDNDCEDDSDETGCGDSHILPFSTPGPSTCPPSQFTCRSTNTCIPAPWRCGDDD  
CEDDSDEEGCSAPASEPPGSL

>IL6#7

CLSSQFQCKNGQCIPQTWVCDGDNDCEDDSDETGCGDSHILPFSTPGPSTCRSNEFQCRSSGICIPRTWVCDGDDD  
CLDNSDEKDAART

>IL6#9

CRSDQFQCGSGHCIPQDWVCDGENDCEDGSDETDCSAPASEPPGSLCLSSQFQCKNGQCIPQTWVCDGDNDCEDDS  
DETGCGDSHILPFSTPGPST

>IL6#P8

CRSDQFQCGSGHCIPQDWVCDGENDCEDGSDETDCSAPASEPPGSLCRSNEFQCRSSGICIPRTWVCDGDDDCLDNS  
DEKDAART

>IL6#N7

CPPSQFTCRSTNTCIPAPWRCGDDDCEDDSDEADCGDSHILPFSTPGPSTCLSSQFQCKNGQCIPQTWVCDGDND  
CEDDSDETGCGDSHILPFSTPGPST--

Please insert the accompanying paper copy of the Sequence Listing, page numbers 1 to 387, at the end of the application.